

Some TNFi Agents Raise Infections Odds More

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Patients taking monoclonal anti-tumor necrosis factor antibody therapy were more likely than those on soluble TNF inhibiting therapy to develop opportunistic infections, other than tuberculosis, in a study of a French national registry.

Of the three TNFi agents used in France in 2004-2007, infliximab was associated with an 18-fold increased risk and adalimumab was associated with a 10-fold increased risk for nontuberculosis opportunistic infection, compared with etanercept. Dr. Dominique Salmon-Ceron and her associates reported. A higher incidence of opportunistic infection with infliximab or adalimumab, compared with etanercept, did not reach

3-year French RATIO (Research Axed on Tolerance of Biotherapies) registry and involved all cases in France of opportunistic infections in patients receiving TNFi agents for any reason. The case-control analysis matched each of the 43 case patients (with a total of 45 opportunistic infections) with 3 control patients who took TNFi agents without developing opportunistic infections.

Patients had been treated with TNFi

agents for RA (26), spondyloarthritis (3), inflammatory colitis (8), psoriasis (1), or other problems (5). Four were on etanercept, 10 received adalimumab, and 39 were on infliximab.

Using pharmaceutical company data, the investigators estimated a total of 57,711 patient-years of use of TNFi therapy during the study period. They calculated an annual incidence of opportunistic infection in patients receiving

TNFi agents as 152 per 100,000 patient-years, after adjusting for age and sex.

The incidence of opportunistic infection differed by TNFi agent, but the differences were not statistically significant (7 per 100,000 patient-years with etanercept, 62 per 100,000 patient-years with adalimumab, and 291 per 100,000 patient-years with infliximab). The rarity of opportunistic infections prevented statistical significance in comparisons. ■

VITALS

Major Finding: Opportunistic infections other than tuberculosis were 18 times more likely in patients on infliximab and 10 times more likely in patients on adalimumab, compared with patients on etanercept.

Data Source: A study of a French national registry of all patients with opportunistic infections while they were on TNFi agents, and case-control analysis of 43 patients with 45 non-TB opportunistic infections and 3 matched control patients without infection on anti-TNF agents.

Disclosures: Some of Dr. Salmon-Ceron's coauthors have been consultants or speakers for Abbott, Schering Plough, UCB, or Wyeth. The study was funded by Abbott, Schering Plough, Wyeth, and INSERM (Institut National de la Santé et de la Recherche Médicale).

statistical significance because of the rarity of the infections. But the findings are supported by previous reports from the Food and Drug Administration, a Spanish registry, a study of 21 Japanese patients, and other accounts of a greater risk for opportunistic infection with infliximab, compared with etanercept, the investigators noted (Ann. Rheum. Dis. 2010 Dec. 21 [doi:10.1136/ard.2010.137422]).

The study also identified a third risk factor: treatment with more than 10 mg/day of oral steroids or IV steroid boluses during the year before a diagnosis of non-TB opportunistic infection. Previous studies also identified this risk factor in patients with rheumatoid arthritis or systemic lupus erythematosus, so the current analysis "strengthens the need to avoid high doses of steroids for patients receiving anti-TNF agents," reported Dr. Salmon-Ceron, who is professor of infectious diseases at Université René Descartes, Paris, as well as a member of the staff at of Hôpital Cochin in that city.

The data in the study come from the



Image of trabecular bone insert reproduced with permission from David W. Dempster, PhD.

INDICATION

Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

❖ **Hypocalcemia:** Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Hypocalcemia may worsen, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Adequately supplement all patients with calcium and vitamin D.

❖ **Serious Infections:** In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® group than in the placebo group. Serious skin infections, as well as infections of

the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia®. Endocarditis was also reported more frequently in Prolia®-treated subjects. The incidence of opportunistic infections was balanced and the overall incidence of infections was similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

❖ **Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in the Prolia® group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

❖ **Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should